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Part I: Treatment of Older Adults: Depression, Anxiety, & Cognitive Problems

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GGEC
Georgia Geriatric Education Center

Part I: Treatment of Older Adults: Depression, Anxiety, & Cognitive Problems

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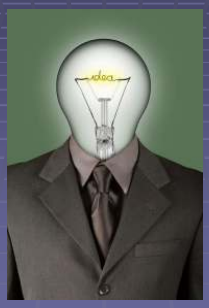
Disclosure Statement:
Dr. Hyer has nothing to disclose.

Big Picture

We suck

Brain Problems

Practice Guidelines



Integrated Care

Aging is complex

Use modules

Careful What you ask for: Clinical Practice Guidelines

79 y/o Female: Osteoporosis, Type 2 Diabetes, Arthritis, HTN, COPD and Depression.

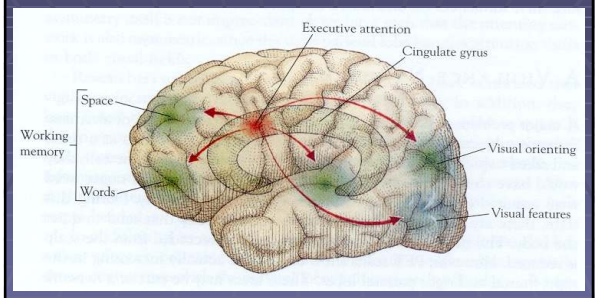
- 13 Meds: 21 times/day
- >$400.00/month
- 18 non-pharmacological activities, such as diet, monitoring
- 6 conditions have 100% chance of drug/drug interactions and 100% for non-pharmacological intervention interactions
- Guidelines do not comment on the time or burden making self management a problem

Boyd et al. JAMA 2005

What are older people like?

Age	% No Disability	% LTC	% Married
65-69	83	3	70
70-74	83	5	60
75-79	78	7	52
80-84	**62**	**10**	**38**
85-89	45	17	24
90-94	35	32	16
95-99	20	42	10
100+	18	48	9

The Brain



Selected Memory Systems

Memory System	Major Anatomical Structures Involved	Length of Storage of Memory	Type of Awareness	Examples
Episodic Memory	Medial temporal lobes, anterior or thalamic nucleus, mamillary body, fornix, prefrontal cortex	Minutes to years	Explicit, declarative	Remembering a short story, what you had for dinner last night, and what you did on your last birthday
Semantic Memory	Inferolateral temporal lobes	Minutes to years	Explicit, declarative	Knowing who was the first president of the United States, the color of a lion, and how a fork differs from a comb
Procedural Memory	Basal ganglia, cerebellum, supplementary motor area	Minutes to years	Explicit, or implicit, nondeclarative	Driving a car with a standard transmission (explicit) and learning the sequence of numbers on a touch-tone phone without trying (implicit)
Working Memory	Phonologic: prefrontal cortex, Broca's area, Wernicke's area Spatial: prefrontal cortex, visual-association areas	Seconds to minutes; information actively rehearsed or manipulated	Explicit, declarative	Phonologic: keeping a phone number "in your head" before dialing Spatial: mentally following a route or rotating an object in your mind

Normal Brain Aging

- Declines
- **Working memory** (keep irrelevant info)
- **Executive Functioning**
- Speed of processing
- Long term memory
- Less controlled processing (elaborative processing)
- Effortful tasks are poor
- Poor source memory
- Senses (visual and verbal)
- Dedifferentiation (less neural specificity)
- Remains OK
- Verbal

Something is going on!

- FDDNP PET used on normal older adults with some depression or anxiety. Half had MCI and half not (N=43).
- MCI and Normals did not differ on depress/anx scores
- MCI:
  Dep→ lateral temporal
  Anxiety→ posterior cingulate
- Normals:
  Dep→ medial temporal
  Anxiety→medial temporal and frontal

There is a relationship between severity of depression and anxiety and FDDNP binding values in non-demented people.

Lavretsky, et al., 2009

Odds Ratios of Neuropathological Features and Dementias at Death

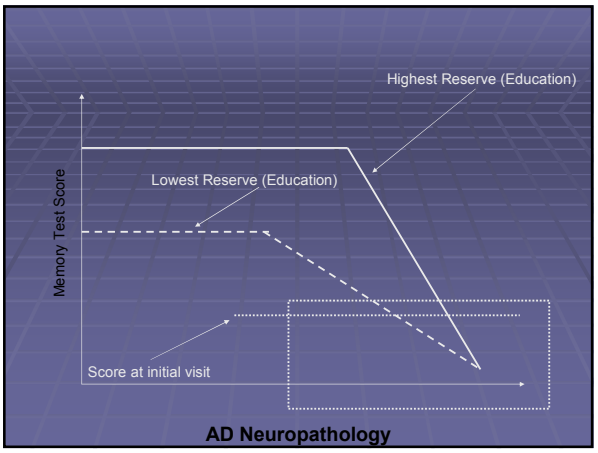
- **Age 75**
- **Neocortical Neuritic plaques** 8.63 (3.81 – 19.60);
- **Neocortical cerebral atrophy** 5.11 (1 –14)

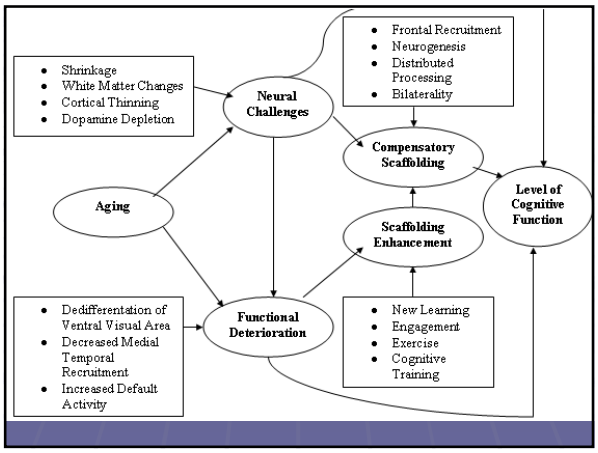
- **Age 95**
- **Neocortical neuritic plaques** 2.48 (.92 – 4.14);
- **Neocortical cerebral atrophy** 6.10 (CI 2 – 13)

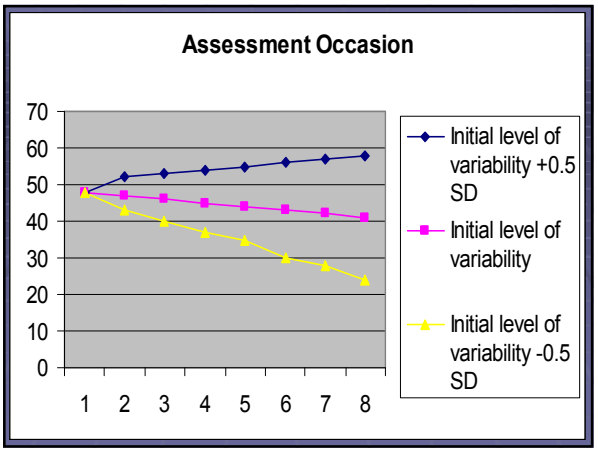
Question 1

Hypotheses of the Aging Brain

- Right brain Hy
- Accelerated aging Hy
- Reverse causation Hy
  (lower IQ declines fast)
- Frontal lobe Hy
- Crystalized and fluid intelligence
- Age 55 marker
- Brain Reserve…..







Older Adults are Own Worst Enemy: Mind Matters

- Internalization of aging stereotypes
- Automatic and unconscious cognitive component (subliminal priming)
- "Old" → negative constructs primed
- Explicit beliefs tend to operate independent of implicit ones
- "My memory lapses are really permanent. "

- Positive priming → increase cognitive performance
- → better handwriting
- → accept life prolonging med interventions
- → gait speed
- → functional health over time; better health utilization and survival
- Negative priming→ stress, cardio markers, depression, etc.

Levy, 2008

The New Psychiatry: Integrated Care

- PRISM-E
- IMPACT
- STAR-D
- PROSPECT
- RESPECT
- UPBEAT

All point to the value and efficacy of integrated care, case management, step care, and value of a planned cognitive/behavioral/ interpersonal intervention.

Gatz, 2007; Oxman, Dietrich, & Schulberg, 2005.

New Psychiatry What? Depression in PCC

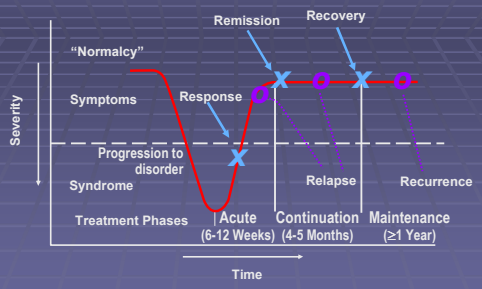
- Meta-analysis of 50,000 across the world
- For every 100 cases:
- 20 true cases
- 10 were correct
- 10 were missed
- 15 non-depressed were seen as depressed
- Varied by countries: US and UK had most problems

Mitchell et al., 2009, Lancet

Psychotherapists are PCPs Who are Competent and Care

- Treatment with meds is a PSYCHOLOGICAL INTERVENTION
- No specific effects of SSRIs and SNRIs; No relationship between dosage and plasma levels of antidepressant and outcome.
- Successful doctors get better results with placebo or SSRIs or whatever.
- It is the Doctor! Create a context and a relationship.

Depression



Kupfer DJ. *J Clin Psychiatry*. 1991;52(suppl 5):28-34. Depression Guideline Panel. Clinical Practice Guideline No. 5: Depression in Primary Care. 2. Treatment of Major Depression. Rockville, Md: Agency for Health Care Policy and Research, U.S. Department of Health and Human Services; 1993. AHCPR publication 93-0551.

Depression

Depression Is different

Brain Problems

Therapies =

Recurrence

Depression shares

Use CBT/PST

Question 2

Consequences of Failing to Achieve Remission

- Increased risk of relapse and treatment resistance[1-3]
- Continued psychosocial limitations[4]
- Decreased ability to work and decreased workplace productivity[5,6]
- Increased cost for medical treatment[6]
- Sustained depression may worsen morbidity/mortality of other conditions[7-9]

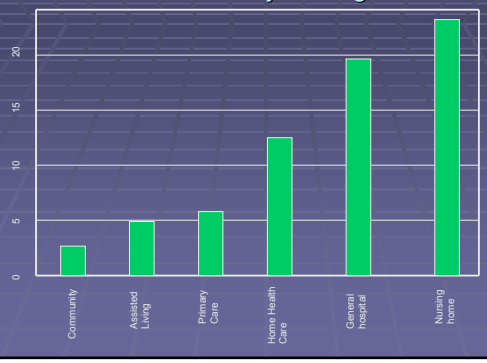
[1]Paykel ES et al. *Psychol Med*. 1995;25:1171-1180. [2]Thase ME et al. *Am J Psychiatry*. 1992;149:1046-1052. [3]Judd LL et al. *J Affect Disord*. 1998;59:97-108. [4]Miller IW et al. *J Clin Psychiatry*. 1998;59:608-619. [5]Simon GE et al. *Gen Hosp Psychiatry*. 2000;22:153-162. [6]Druss BG et al. *Am J Psychiatry*. 2001;158:731-734. [7]Frasure-Smith N et al. *JAMA*. 1993;270:1819-1825. [8]Penninx BW et al. *Arch Gen Psychiatry*. 2001;58:221-227. [9]Rovner BW et al. *JAMA*. 1991;265:993-996.

Prevalence of Depression and Anxiety

- Representative estimates of mood, anxiety and combined mood and anxiety disorders using a sample of 2,575 survey participants age 55 and older.
- 43% 55 to 64; 32% 65 to 74; 20% 75 to 84 years; 5% >85.
- **5% mood disorder within the previous year.**
- **12% anxiety disorders (all)**
- **3% mood and anxiety disorders.**
- Prevalence of all the conditions declined with age.
- 55 to 64 vs > 85, 7.6% vs. 2.4% mood disorders;
  16.6% vs. 8.1% anxiety disorders;
  4.8% vs. 0% both conditions.
- Women were more likely to have any of the disorders than men

Byers et al., 2010 May *Archives of General Psychiatry*

Prevalence of Major Depression in Older Adults By Setting



Depression: 5 Years

- Response Yes…Remission NO
- Subsyndromal states (MinD, SSD)
- Case Management/CBT
- PCC→ Importance of Medical Care
- Importance of Anxiety
- Executive functioning
- Suicide: Black Boxes +
- Scans
- Pharmaco-genetics (?)

Response and Remission in Depression

- Response
  - significant improvement but not necessarily complete relief of symptoms
  - often measured by ≥50% decrease from baseline HAM-D score
- Remission
  - minimal or no symptoms
  - return to functional normality
  - no longer meets diagnostic criteria
  - often measured as HAM-D of 7 or less

Frank E et al. *Arch Gen Psychiatry*. 1991;48:851-855.
Rush AJ, Trivedi MH. *Psychiatr Ann*. 1995;25:704-709.

Geriatric Depression

Symptom	Adult Presentation	Geriatric Presentation
Mood	Depressed Anhedonic Suicidal Thoughts	Weary, Hopeless, less Anger, Anxious Thoughts of Death
Somatic	↓↑ Sleep ↓↑ Appetite ↓↑ Psychomotor ↓↑ Increased Pain	↑ Pain, and Somatic symptoms overlap with effects of medications, comorbid disease
Cognitive	↓ Concentration Indecisiveness	Decrease in: Selective attention Working memory/retrieval New learning Processing speed Executive function

Gallo et al. 1997; Geiselmann and Bauer 2000; Devanand 1994;

What is going on? Typical biomarkers

NO BIOLOGICAL MARKER
But….. But….

- Twin studies (16% of variance in CES-D and 19% of somatic items)
- White matter hyperintensities
- 5HT2A and 5HT1A receptor binding decreases: Increased incidence of homozygous "short" alleles in promoter region of 5-HT transporter
- CRF hypersecretes
- HAM-D Factor correlates with distinct brain regions.
- Weight loss
- Cardiovascular disease
- Platelet activation is >
- T-cell response is lower
- Poorest blastogenic response to mitogens
- Highest level of cytokine interleukin 6
- Elevated homocysteine levels

Depression Manifesto

- "Advances in knowledge in the psychopathology of mood disorders seem to make it clear that the wrong target has been addressed. That is, it is now known that the major depressive episodes will respond to most reasonable treatments in the short term or will remit on their own, but they will **almost always recur**. To be truly effective, treatments, whether psychological or pharmacological, must prevent recurrence of future depressive episodes."

Barlow, American Psychologist 2004 (p.873)

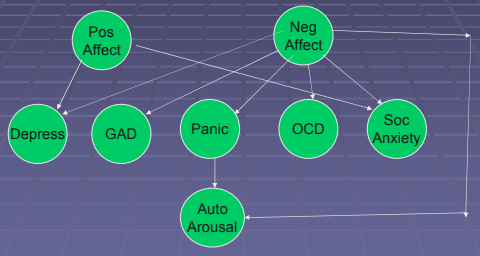
Shades of Gray

- Minor depression: 2-4 symptoms, low mood or anhedonia
- Subsyndromal depression: 16 on CES-D
- Mixed Dep and Anx
- Depression without sadness
- Bereavement
- Depressive Executive Dysfunction
- Depression in dementia
- Post Stroke depression
- Suicidal Depression: Fatigue, Hopelessness and Negative Outlook (Joiner, et al., 2001)

More Depression Mystery

- Depression as adaptation: Fever is a metaphor. Depression promotes an analytic thinking style.
- Depression as dimension: Is there evidence of a break at 4-5 symptoms?
- Depression as excessive: Real prevalence is 1-2%.
- Depression as a latent variable: Slade and Andrews (2005): using taxometric analysis→ whether a construct is better considered as two latent discrete variables or one latent continuous variable.

Big Picture



And then there is this…

- "There is increasing evidence that symptoms of elderly depression may be etiologically distinct (e.g, more psychomotor retardation and anhedonia in vascular depression) and that focusing on subclusters of depressive symptoms, rather than relying on general depression assessment tools may help enhance construct validity…" (p.379)
- At the least, "It is apparent that the 'oldest old' (>75) present different from the 'young old.'" (p. 379)
- At the least, "…the development of depression and cardiovascular dysfunction share molecular mechanisms, such as stress induced changes in inflammatory markers and neurotransmitter signaling, all related to common genetic elements." (p. 380)

Lu & Ahmed, 2010 AJGP, p. 379.

Factors in Depression Rx

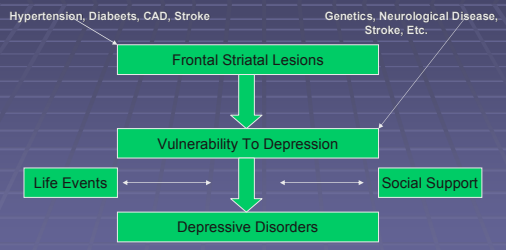
Question 3

Small Cerebral Infarcts and Depression

- Documented in MDD 2 decades ago
  - Coffey et al, 1987
- In over 50% of patients with late onset MDD
  - Fujikawa et al, 1993
- Akin to the white and gray matter hyperintensities
- SCI/Hyperintensities associated with:
  - More severe symptoms
  - More hospital admissions for depression
  - Longer hospitalizations for depression
  - Resistant to meds
  - EF problems

Alexopoulos et al, 1997; Steffens et al, 2003

Development of Late Life Depressive Disorders



Model of Risk Factors That Lead to Depressive Disorders

Adapted from Krishnan KRR. Biol Psychiatry. 2002; 52: 185-192

Frontal Lobe Hypothesis of Aging

Occur in the absence of disease, stroke, or neurotoxic events in otherwise healthy brains.

Basic cognitive skills left intact.

We are simply outliving our brains.

MRI Changes in Late-Life Depression

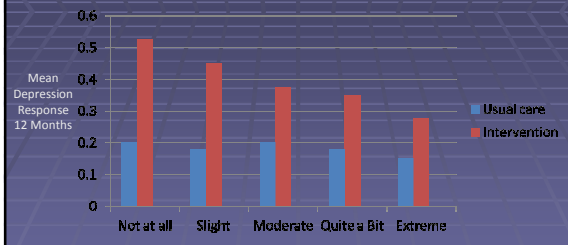
- Enlargement of lateral ventricles
- Cortical atrophy
- Increased incidence of periventricular hyperintensity
- Increased incidence of deep white-matter lesions
- Increased incidence of basal ganglia lesions
- Smaller caudate nucleus
- Smaller putamen nucleus

Problem: Depression of Alzheimer's Disease

- Symptom profile not typical (heterosyndromal)
  - Symptoms fluctuate often, may be transient in short term
  - Anhedonia, irritability, anxiety, nonspecific worry
  - Prominent apathy, neurovegetative change
  - Frequent "psychotic" features, esp. delusions (30% to 40%)
  - Guilt, self-blame less common; suicidality rare

Zubenko GS, et al. Am J Psychiatry. 2003; 160: 857-866
Lyketsos CG, et al. J Neuropsychiatry Clinical Neurosci. 1997; 9: 556-561

DYK: Pain Impedes Improvements in Depression

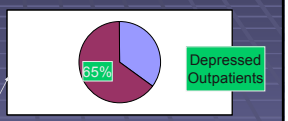


Baseline Pain Interference

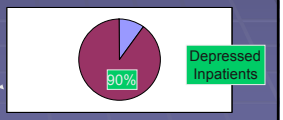
Thielke SM, et al. *Am J Geriatr Psychiatry*. 2007;15(8):699-707.

DYK: Depression and Insomnia Coexist

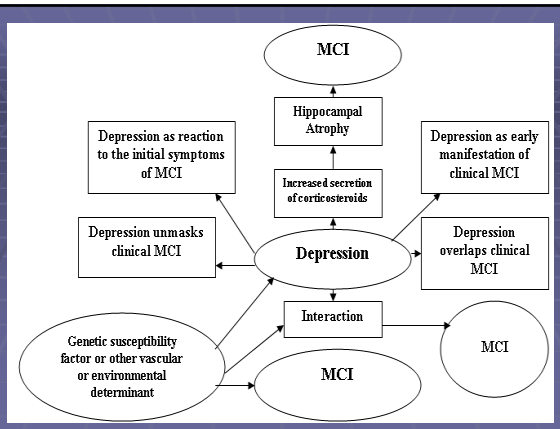
Roughly 65% of outpatients and 90% of inpatients with major depression also have insomnia



Comorbid Insomnia



Nowell and Buysse. *Depress Anxiety.* 2001; 14(1):7-18.



Outcomes for Depression

Meds: Treatment Matters (?)

- 2007 ApA Meeting with 1066 psychiatrists
- One third said that current antidepressants are only "somewhat effective."
- Biggest Problems:
  - Sexual dysfunction,
  - Weight gain,
  - Inadequate efficacy

Olin. 2007

Depression meds: Patients report 20 times more side effects than recorded in charts (Zimmerman, 2010). TSES was used on 300 patients. Patients rated frequency of 31 side effects.

Combination Wins!

- *Compared antidepressant med alone with antidepressant treatment in combo with a psychological intervention in MDD*
- *16 studies, 932 patients randomized to pharmacotherapy and 910 to combined.*
- *Results: < 12 Weeks:*
  Combined vs drug OR = 1.86:

  > 12 weeks
  Combined vs Drug OR = 2.2

- *No significant effect for meds alone*
- *Studies not affected by study quality*

Pampallona et al. (2004)

Response to Depression is a Placebo Response

- Meta-analysis: Acute phase, parallel group, double blinded, placebo controlled with random assignment, for 2nd generation antidepressants not associated with a med disorder and 60 or >. Cochrane and Medline
- 10 unique trials with 13 contrasts (N=2377 active drug and 1788 placebo)

- **Response rates for Drug = 44.4%**
- **Response rate for Placebo=34.7%**
- **Placebo rates vary 19-47%. Lots of heterogeneity: Nonspecific effects**
- **10-12 weeks > 6-8 weeks**

- **Oh boy…. For every 100 treated,**
  8 show a response and
  5 show remission in excess of placebo

Nelson et al., 2009

What about Meds and Depression?

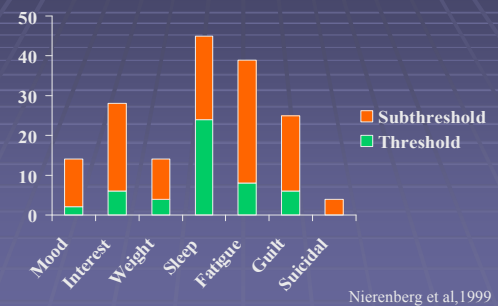
- Only 33% full remission (Ham <7): Residual symptoms usual
- Pain/Physical symptoms are part of picture
- 25%- 30% dropout: Intent-to-Treat
- High relapse rates
- Less QoL
- What to export?

  Needs something more than meds

Remission Rates

- National Comorbidity Survey Replication treatment rate: 42%
- IMPACT (1801) and PROSPECT (517): < ½ experienced 50% reduction in symptoms.
- IMPACT: ¼ in full remission
- Cognitive Therapy: 45.8% (ITT) (DeMaat et al., 2006)
- CBT: <25% Westen & Morrison (2001) (ITT)

Residual symptoms in depressed patients after response to fluoxetine



Nierenberg et al,1999

Question 4

Predictors of Response to Antidepressants or Placebo + Clinical Management

- The literature suggests that the following are associated with reduced response:
  - Older age (>75 years)
  - Lesser severity (≤ median baseline HAMD)
  - Single episode (vs. recurrent)
  - Late onset (≥ 60 years)
  - Anxious depression (HAMD anxious factor)
  - Cognitive impairment (MMSE < 24)
- Gender was also examined

Nelson, et al. Presented at AAGP 2009.

Overall Statement

- "The good news is that most psychotherapies developed for younger patients appear useful for older adults when applied in an age-informed and age-sensitive manner."

Henrichsen, 2008; Knight, 2004; Scogin et al, 2005

- Aging Challenge: Assimilation and Accommodation

Recent Psychosocial Projects

- Depression (Number of Studies)
  - PST (11)
  - CBT (2)
  - Behavioral activation in home/nursing home (2)
  - Family/couples involvement in care (2)
  - Collaborative care (3), including nonpharmacologic care (1)
  - Complementary therapy (1)
- Anxiety (Number of Studies)
  - CBT and PST (5), including generalized anxiety disorder (GAD) (3)
  - PTSD (1)
  - GAD (1)
  - Nonpharmacologic therapy (3)

Wetherell, AAGP

Question 5

Exercise

- Overall health:
  - Helps if in 40-60 (WHI)
  - Helps if cardiac problems
  - Helps if want better QoL
- Cognition Health
  - Helps if 40-70
  - Helps if 70-90, sedentary
  - Helps if 70-90, active
  - Helps with EF/frontal
  - Lower risk of AD
  - Improves RT/balance
- Depression
  All ages, anything reduces relapse
- What helps:
  Anything over baseline
  Best 30-60 minutes/day
  Increases serotonin and neuroepinephrine and BDNF
- "Exercise is a reasonable alternative to antidepressants"

  Bartholomew & Cicolo, 2007
- Increases BDNF in hippocampal tissue.

Small, 2008

Mercer Recommendations for Depression Interventions

- Use combination therapy -- Med and Psychosocial therapies
- Usual assessment but also assess for EF
- Psychosocial effective first-line treatments include
  - Behavioral activation
  - PST
  - CBT
- Use case manager
- Exercise
- Problem: Comorbid depression/anxiety: treat depression first

Cognitive Behavioral Therapy (CBT) for Depression

- Behavioral activation
  - Develop a list of pleasant activities
  - Do at least one BA per day
  - Rate mood before and after
- Changing negative automatic thoughts (e. g., overgeneralization, "shoulds")
  - Identify the negative thought
  - Identify evidence for and against
  - Create a more realistic alternative thought
- Typically 12 to 20 sessions (6 to 8 for behavioral activation alone)
- Extensive literature in outpatient mental health, medical, homebound, and cognitively impaired samples

ESTish Treatments of Depression

- CBT (Beck)
- Control Your Depression (Lewensohn)
- Behavioral Activation (Martells et al)
- IPT (Klerman & Weissman)
- Problem Solving (Arean; Nezu)
- Mindfulness (Teasdale) /ACT (Hayes)
- Interesting ideas: Interactional Problems (Coyne); Control; Ruminative styles; AIF

Assessment

- Overall:
- Assess medical and psychiatric comorbidities. Charlson Index
- Assess social support, cognition, sensory, sleep, pain, meds
- Consider omnibus Measure: MBMD, PAI, NEO-PI
- Clinician Ratings
  HAM-D (17 or 24, use 10), MINI, PHQ-2, GDRS (use 20), MADRS
- Self Report scales
  PHQ-9, BDI-I or II (10), GDS (11), GDS-SF (5), CESD (20 item, cut-off 16: 10 item, use 10), Zung Depression Self Rating Scale (50), Visual Analogue Mood Scales
- Dementia and Depression
  Cornell Scale for Depression in Dementia (19 items use to get severity after depression is established), Dementia Mood Assessment Scale (17 items), Provisional Depression in Dementia (Olin et al., 2002)

Screening Tools: PHQ-9

- Older adults: PHQ-9 has 88% sensitivity and 88% specificity (Kroenke et al. 2001)
- Use PHQ-2 and score of 3 or more (0-6)
- Then use PHQ-9 and use 10 or > (0-27)

- PHQ-2 is a quick depression screen
  In past 2 weeks, have you been bothered by:
  - Little interest or pleasure in doing things?
  - Feeling down, depressed or hopeless?

Treatment of Older Adults: Depression, Anxiety, & Cognitive Problems Pt. 1

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Evaluation

To complete the evaluation, click on the survey link below or paste the link into your web browser.

www.surveymonkey.com/s/geriatric1

This evaluation must be completed in order to receive contact hours/certificate.